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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,832	08/28/2001	Michele A. McTigue	0125-0016D2	3870

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/939,832	MCTIGUE ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action responds the Amendment received on November 4, 2003.

Sequence Rules

The objection to the specification for failing to comply with the Sequence Rules as set forth in 37 CFR 1.82(a)(1) and (a)(2), wherein the specification disclosed an oligonucleotide sequences without its SEQ ID Number, made in the Office Action mailed on August 7, 2003 is withdrawn in view of the Amendment received on November 4, 2003, amending the specification to recite the proper SEQ ID Number.

Information Disclosure Statement

The Examiner of record acknowledges the oversight of not initialing references AA1 through AD1, in the IDS received on October 1, 2001. A signed PTO-1449 correcting this deficiency is attached hereto.

Claim Objections

The objection of claims 17, 24, 25, and 26 for failing to first identifying the acronyms, "RTK," "PDGFR," and "VEGFR," without first describing them, made in the Office Action mailed on August 7, 2003 is withdrawn in view of the Amendment received on November 4, 2003.

Claim Rejections - 35 USC § 112

The rejection of claims 17-27 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter, made in the Office Action mailed on August 7, 2003 is withdrawn in view of the Amendment received on November 4, 2003.

Rejection – Written Description; Necessitated by Amendment

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicants' newly submitted claims 28 and 29, wherein the claims now require that the modified RTK polypeptide be selected from a Markush Group of polypeptides which excludes that which was cited in the prior art in the Office Action mailed on August 7, 2003 (Williams et al.), necessitates the instant rejection.

Claims 28 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description Rejection.

Instant claims are drawn to a method of identifying compounds which interact with the kinase domain of a modified tyronsine kinase polypeptide, wherein the modified tyrosine kinase polypeptide is selected from the group consisting of IRK, FGFR-1, and VEGFR-2 (instant claim 28); or wherein the modified tyrosine kinase polypeptide is vascular endothelial growth factor (VEGFR) polypeptide (instant claim 29).

The written description analysis for each claim is separately addressed.

Modified IRK, FGFR-1, and VEGFR-2

Instant claim 28 requires the use of a RTK gene construct which comprises a truncated KID that links domain α helix D and α helix E, the construct of which encodes a modified RTK

polypeptide that, "forms crystals suitable for x-ray crystallography." Such modified RTK polypeptide is recited as being selected from the group consisting of insulin receptor (IRK), fibroblast growth factor receptor-1 (FGFR-1) and vascular endothelial growth factor receptor-2 (VEGFR-2).

The claim fails to fully describe the subgenus encompassed by the instant claim for the following reasons.

The specification only discloses a single species of modified VEGFR-2, wherein the modification comprises 50 residue-deletions from a kinase insert domain, identified by SEQ ID NO: 5. However, the specification does not give any example or disclosure regarding other species of modified RTK polypeptides recited in the Markush Group, *i.e.,* FGFR-1 and IRK. Further, the specification does not give any disclosure or examples of whether, if such modified polypeptides were to be produced for the claimed FGFR-1 and IRK, the modified polypeptides would "form crystals suitable for x-ray crystallography" as claimed in instant claim 28.

In *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998), the court stated that, "the 'essential goal' of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed."

MPEP 2163(I) states that an applicants may show possession of the claimed invention in a variety of ways including description of actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

The specification only discloses the x-ray crystallography coordinates (derived from a crystallized structure) of the modified VEGFR-2 polypeptide comprising the deletion of 50 residues in the KID represented in SEQ ID NO: 5 (also identified as VEGFR-2Δ50 (Figure 7)). All of the examples and description point to a single species of VEGFR-2Δ50, such as isolation of the gene construct encoding the modified polypeptide (pages 11-12), the isolation and purification of the modified polypeptide (page 13), the kinetic assays (page 14, top), ***crystallization*** of the modified polypeptide (pages 16-20), structural determination (page 18). The specification lacks the evidence of reduction to practice for modified polypeptide of the species of IRK and FGFR-1, nor does the specification disclose the structure of these species comprising the claimed truncation as well as their crystallized coordinates. Therefore, a skilled artisan would not be able to recognize that Applicants, at the time the application was filed, was in possession of a modified polypeptide comprising a truncated KID, which forms crystals suitable for x-ray crystallography, wherein said modified polypeptide is IRK or FGFR-1.

Modified VEGFR

Instant claim 29 requires the use of a RTK gene construct which comprises a truncated KID that links domain α helix D and α helix E, which encodes a modified RTK polypeptide that, "forms crystals suitable for x-ray crystallography," wherein said modified RTK polypeptide encompasses the subgenus of modified VEGFR polypeptides

The claim fails to fully describe the subgenus that is encompassed by the instant claim for the following reasons.

The claim encompasses the species of modified VEGFR-1 polypeptide comprising a truncated KID, wherein the modified polypeptide forms crystals suitable for x-ray

crystallography. However, the specification only discloses a single species of modified VEGFR-2, wherein the modification comprises 50 residue-deletions a kinase insert domain, identified by SEQ ID NO: 5. The specification does not give any example or disclosure regarding the species encompassed by the subgenus claim, which extends to a modified VEGFR-1 polypeptide that comprises the recited truncation of the KID. Further, the specification does not give any disclosure or examples of whether, if such modified polypeptide were to be produced for VEGFR-1, the modified polypeptide would "form crystals suitable for x-ray crystallography" as claimed in instant claim 29.

In *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1566, 43 USPQ2d 1398, 1404 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089 (1998), the court stated that, "the 'essential goal' of the description of the invention requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed."

MPEP 2163(I) states that an applicants may show possession of the claimed invention in a variety of ways including description of actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention.

The specification only discloses the x-ray crystallography coordinates of the modified VEGFR-2 polypeptide (derived from its crystallized structure) comprising the deletion of 50 residues in the KID represented in SEQ ID NO: 5 (also identified as VEGFR-2Δ50 (Figure 7)). All of the examples and description point to a single species of VEGFR-2Δ50, such as isolation of the gene construct encoding the modified polypeptide (pages 11-12), the isolation and

purification of the modified polypeptide (page 13), the kinetic assays (page 14, top), ***crystallization*** of the modified polypeptide (pages 16-20), structural determination (page 18). The specification lacks the reduction to practice for modified polypeptide of VEGFR-1, nor does the specification disclose the structure of this species comprising the claimed truncation as well as its crystallized coordinates, to serve as evidence to a skilled artisan that Applicants, at the time the application was filed, was in possession of a modified VEGFR-1 polypeptide comprising a truncated KID, which forms crystals suitable for x-ray crystallography.

Additionally, according to Applicants' response on page 8, it appears that Applicants are stating that not every polypeptide is able to form crystals suitable for x-ray crystallization. Based on such argument, coupled with the absence of any disclosure or examples in the specification, it would further serve as evidence to a skilled artisan that Applicants, at the time the application was filed, had possession of modified VEGFR-1 polypeptide, wherein said polypeptide is able to form crystals suitable for x-ray crystallization.

Claim Rejections - 35 USC § 102 - Maintained

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 17-24 under 35 U.S.C. 102(e) as being anticipated by Williams et al. (U.S. Patent No. 6,043,211, issued March 28, 2000, filed June 5, 1995), made in the Office Action mailed on August 7, 2003 is maintained for the reasons of record.

Applicants' arguments received on November 4, 2003 have been fully considered but they are not found persuasive for the reasons of record.

Applicants' arguments are addressed in the order they were received.

Applicants appear to argue that, "the passing reference to x-ray crystallography does not teach or suggest that the mutated protein of Williams is in fact suitable for x-ray crystallography; i.e., that the mutated protein has properties that will allow the protein to crystallize," (on page 8, 1st paragraph).

Applicants' assertion has been noted. However, Applicants have not provided any evidence to shift the burden on the Office that the modified protein of Williams would, in fact, not crystallize. Applicants' claims are drawn a method of using a modified RTK polypeptide, wherein the modified polypeptide comprises a truncated Kinase Insert Domain (KID). As already set forth in the previous Office Action mailed on August 7, 2003, the modified polypeptide disclosed by Williams et al. comprises characteristics which are the same as that which is described by Applicants, that is, a polypeptide comprising a modified PDGFR-β which comprises deletion (or truncated) KI region (or kinase insert domain) (column 46, lines 23-25).

According to *In re Best* 195 USPQ 430, 1997, the court stated that, "Patent Office can require applicant to ***prove*** that prior art products do not necessarily or inherently posses characteristics of his claimed product wherein claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes; ***burden of proof is on applicant***" (pp. 430). Since the polypeptide employed by Williams et al. comprise a truncated domain in the Kinase Insert Domain, while retaining its kinase activity, evidencing that the kinase domain is of sufficient length to maintain conformation associated

with kinase structure (column 46, line 25), and Applicants have failed to provide evidence to the contrary, as set forth in *In re Best*, such polypeptide would be structurally similar to that which is claimed in the instant claims, therefore, able to form crystals.

Additionally, if Applicants would argue that crystallization of proteins is delicate and not applicable to any proteins, and prove that the protein of Williams et al. would not crystallize, Applicants are advised that the instant claims are drawn to a subgenus of modified RTK polypeptides which comprise a truncation in the KID, wherein the subgenus of polypeptides **must** crystallize. As the instant specification only discloses a single species, VEGFR-2 comprising 50 amino acids residues in the KID domain, as defined by SEQ ID NO: 5, such argument would subject the instant claims under examination under Written Description requirement.

Claim Rejections - 35 USC § 103 - Maintained

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 20 and 21 under 35 U.S.C. 103(a) as being unpatentable over Williams et al. (U.S. Patent No. 6,043,211, issued March 28, 2000, filed June 5, 1995), made in the Office Action mailed on August 7, 2003 is maintained for the reasons of record.

Applicants' arguments received on November 4, 2003 have been fully considered but they are not found persuasive for the following reasons.

Applicants arguments drawn to the instant rejection under 103(a) is dependent on the whether Williams et al. teach the claimed invention, the argument of which have already been addressed above.

Therefore, the rejection is maintained for the reasons of record.

Double Patenting

The provisional obviousness-double patenting rejection of claims 25 and 26 as being unpatentable over claim 3 of copending Application Serial Number 09/939,833, 09/939,932, and 09/939,764, made in the Office Action mailed on August 7, 2003 is withdrawn in view of the arguments presented (and upon verification) in the Amendment received on November 4, 2003, arguing that claim 3 have been cancelled in their preliminary amendment.

Examiner acknowledges that '832 application **is** the instant application, and was an oversight. In response to Applicants' inquiry regarding 09/506,906 application. The '906 application is not subjected under double patenting rejection.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner can normally be reached from 8:30 a.m. to 6:00 p.m. Monday through Thursday. If attempts to reach the Examiner by telephone are unsuccessful, the Primary Examiner in charge of the prosecution, Dr. Kenneth Horlick, can be reached at (571) 272-0784. If the attempts to reach the above Examiners are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782. Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (703) 872-9306. For Unofficial documents, faxes can be sent directly to the Examiner at (517) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0507.

Young J. Kim
Patent Examiner
Art Unit 1637
1/28/04

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
2/4/04